Mammalian Toxicity of Lunar Dust and Related Simulants

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Summary

- Framing the health risk assessment problem for Lunar dust
- Descriptive toxicology
- U.S. results on Apollo samples
- Russian results on Luna samples
- Findings on Lunar dust simulants
- Conclusions and look ahead

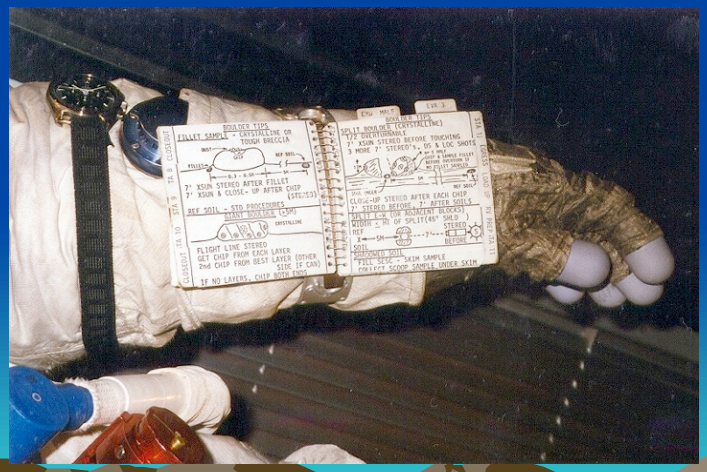
Framing the Risk Assessment Problem for Lunar Dust

- How much could toxicity vary from site to site on the moon?
- What is the potential for human exposure to dust within the habitat?
- How important is size distribution & reduced gravity → depth of penetration into lung
- What is the impact of shape & surface area variations of dust particles → pulmonary response
- Will the mineral content of particles affect bioavailability?
- How reactive is the particle surface and how quickly can the reactivity be lost when particle enters the habitat?
- Is there potential for translocation of particles to other sites within the body?
- What descriptive toxicity data do we already have?

Potential for Toxicity Differences in Soil from Site to Site

- Remain focused on respirable fraction
- Worry about reactive surfaces
- Mechanical processes: destructive and constructive
- Environmental processes: solar & cosmic particles striking surface → maturation
- Addition of meteoritic component → maturation
- Agglutinates (5-65% of soil), iron rich
- Size distribution varies (40-800 um means)
- Depth variations could be important
- Chemical variations: reference suite <10um (Tables 17.16/17.17, McKay)
  - Ni 450-2700 ppm* **Co 75-890 ppm** Sr 80-290 ppm
  - **Ce 15-200 ppm** **Nd 10-120 ppm**
  - SiO_2 41.3-48.5 % **TiO_2 0.3-7.3 %** Al_2O_3 15.6-28.6 %
  - FeO 4.3-15.1 % MgO 4.3-9.8 % CaO 11.3-16.5 %
  - Na_2O 0.36-0.73 % K_2O 0.07-0.59 % MnO 0.06-0.18 % Cr_2O_3 0.1-0.4 %

Potential for Dust to Enter the Habitat



- After lunar EVA the crewmen and the samples they had collected were covered with fine lunar material. Despite attempts at cleanup and packaging in the LM, transfer of crew and materials back to the CM resulted in contamination of the CM atmosphere (Brady et. al, 1975)
- The lunar surface has a layer of fine particles that are easily disturbed and placed into suspension. These particles cling to all surfaces and pose serious challenges for the utility of construction equipment, air locks, and all exposed surfaces (Slane ’94)
- Dust particles levitated at the lunar terminator, perhaps due to polarity changes (Criswell ’72).

Size Distribution and Lung Penetration in Reduced gravity

- Moon's gravity about 1/6 th earth
- Sedimentation is affected by G level
- For 1 um particles and a penetration volume of 800 ml the (Darquenne, 99)
  - % deposition at 1 G was about 41%
  - % deposition at 0 G was about 34%
  - Gravity controlled differences in particle deposition may have a small effect compared to other unknowns such as dust composition (2-10 fold), individual susceptibility (2 fold), species extrapolation uncertainty (3 fold), and relevancy of toxic endpoints (10 fold).

Effect of Particle Shape and Surface Area on Pulmonary Response

- Jagged or elongated shapes tend to be more toxic than amorphous particles
- For insoluble particles the biologic response appears to be driven more by surface area (m^2/kg body weight) than dose to the lungs in mg/kg body weight.

Is the Mineral Content Bioavailable or is the Surface Reactive?

- Surface reactivity can profoundly affect the toxicity of particles.
- Is the surface of lunar dust particles rendered reactive by their environment?
- If the particle surfaces are reactive, then how stable is the reactivity in an environment that supports life?
- Is the reactivity lost if a dust sample is returned to earth?

Is There Potential for Translocation within the Host?

- What portion of lunar dust is in the ultrafine range?
- Can transport occur from the nasal passages into the brain?
- Can transport occur from the respiratory system into the cardiovascular system?
- Are there other plausible transport routes?

Descriptive Toxicology: The Pros and Cons of Intratracheal Instillation

- Pros
  - Cheap/easy/use less material
  - Accurate dosage
  - Calibrate against known compounds
  - No concomitant oral/dermal exposures
  - Bypasses the efficient nasal filtering apparatus of rodents
- Cons
  - Unnatural route/vehicle effects/bioavailability increased
  - Deeper penetration/slowed clearance/exaggerated response
  - Can’t detect effects on upper airways
  - Careless choice of dose can cause lung overload

Checklist for Completeness of a Toxicity Study

- Test material is well characterized and delivered in an inert vehicle
- Test species is appropriate model for human response
- Route of administration is relevant to potential exposure conditions
- Several dose levels are administered and a sham control group is evaluated
- Sufficient numbers of test animals per test group are employed
- Toxic endpoints are relevant, assessed at the appropriate time, objectively measured, and tested by appropriate statistical methods

Descriptive Toxicity of Lunar Dust: Testing on Apollo-returned Samples

- Holland and Simmonds (72) reported intratracheal instillation to small groups of guinea pigs of 20 mg of a pooled sample suspended in 2 ml of sterile saline. The animals were killed 2 or 4 days later for pathology evaluation. The investigators report alveolar cell hypertrophy, septal edema, mononuclear infiltration, and macrophage proliferation around spikules of dust; however, the control and dosed animals had a "significant degree" of spontaneous pathology that confounded the results. The authors conclude that additional studies are needed. The study as reported did not meet many of the criteria for a credible toxicity study.

Descriptive Toxicity of Lunar Dust: Testing on Luna-returned Samples

- Kustov et. al (‘74) and Antipov et. al (74) reported exposing mice 4 h/d for 4 d to air passed over lunar surface material. Various behavioral, hematological, physiological, and pathological endpoints were deemed to be negative. The experiments as reported violate almost all the criteria for a credible toxicity study
- Batsura et. al. (‘81) reported intratracheal administration of 50 mg of lunar soil to white rats and looking at the cellular and pathological effects on their lungs 3 d, 3 mo, and 6 mo later. They reported evidence of inflammation, particle migration to adjacent tissue, and fibrotic changes. This study as reported violates almost all the criteria for a credible toxicity study.
- Kustov et. al. (‘81) reported intratracheal administration of 50 mg of Lunar soil, SiO_2, or vehicle control to Wistar rats. Clinical and physiological observations were done over 6 mos, and then the rats were killed for pathology studies. The investigators report subnormal weight gain, decreased blood parameters, evidence of fibrogenic effects, and increased lung weights. The severity was much less than in the SiO_2 positive control. The massive dose and haphazard way in which this experiment was reported render it of little value in understanding the potential toxic response of the lung to lunar dust.

Non-Respiratory Toxicity of Lunar Samples: Russian

- Antipov (’74) oral administration of supernatant or ip administration of suspended dust did not decrease 6-month survival of mice.
- It is unclear to me whether either of the above administrations enhanced the tumorigenic tendencies of radiation

Non-respiratory Toxicity of Lunar Samples: American Studies

- Holland and Simmonds (’72) and Taylor (’75): lunar material injected IP into mice caused low grade inflammation; particles were transported to lymph nodes. No fibrosis was noted after 16 days. Material persisted for the life of the animals (20 months)
- SC injection led to low grade inflammation, which resolved in a few days to leave a few lesions after 15 d.

Testing on Lunar Dust Simulants

- Lam et. al (02 a,b) reported intracheal instillation of JSC-1 lunar soil simulant to mice at doses of 0.1 or 1 mg in saline. Saline, TiO_2 and SiO_2 at comparable doses were also administered to mice. Mice were killed at 4 h, 24 h, 7 d or 90 d after instillation and evaluated for biomarkers in lavage fluid (early sacrifices) or pathological changes (late sacrifices). The only cellular increase was in the fraction of neutrophils in the lavage fluid after 24 h; the percent increase over controls was present in the 0.1 (14%) and 1 mg (30%) groups. Pathology studies showed a mild increase in macrophages in the low dose group at 7 d, and it showed mild inflammation in the 7 d and 90-d groups at high dose. Mild fibrosis was present in the high dose group after 90 d. In the low dose group the lunar simulant was cleared by 90 d and the tissue was normal appearing. Overall the lunar simulant was somewhat more toxic than TiO_2 and much less toxic than SiO_2.
- Was the 0.1 mg group without ***adverse*** effects?

Conclusions and Look Ahead

- We must determine whether transient surface activation is important and persists in a habitat.
- We must carefully devise a plan to evaluate and understand site variations in toxicity.
- We need to better characterize the nature of particles of < 10 um.
- We need to understand the acute and chronic toxicity of lunar dust, and know if translocation within the body is possible.